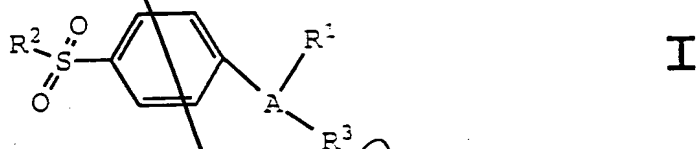


What is claimed is :

1. A method to suppress immune, acute or delayed-type hypersensitivity response in a subject, said method comprising treating the subject with a therapeutically-effective amount of a 5-lipoxygenase inhibitor and a cyclooxygenase-2 inhibitor selected from Dupont Dup 697, Taisho NS-398, meloxicam, flosulide and compounds of Formula I



wherein A is a 5- or 6-member ring substituent selected from partially unsaturated or unsaturated heterocyclo and carbocyclic rings;

wherein R¹ is at least one substituent selected from heterocyclo, cycloalkyl, cycloalkenyl and aryl, wherein R¹ is optionally substituted at a substitutable position with one or more radicals selected from alkyl, haloalkyl, cyano, carboxyl, alkoxycarbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, arylamino, nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy and alkylthio;

wherein R² is selected from alkyl, and amino; and

wherein R³ is a radical selected from halo, alkyl, alkenyl, alkynyl, oxo, cyano, carboxyl, cyanoalkyl, heterocycloxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkyl, aryl, haloalkyl, heterocyclo, cycloalkenyl, aralkyl, heterocycloalkyl, acyl, alkylthioalkyl, hydroxyalkyl, alkoxycarbonyl, arylcarbonyl, aralkylcarbonyl, aralkenyl, alkoxyalkyl, arylthioalkyl, aryloxyalkyl, aralkylthioalkyl, aralkoxyalkyl, alkoxyaralkoxyalkyl, alkoxycarbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-arylaminocarbonyl, N-alkyl-N-arylaminocarbonyl,

alkylaminocarbonylalkyl, carboxyalkyl, alkylamino, N-aryl amino, N-aralkyl amino, N-alkyl-N-aralkyl amino, N-alkyl-N-aryl amino, aminoalkyl, alkylaminoalkyl, N-aryl aminoalkyl, N-aralkyl aminoalkyl, N-alkyl-N-aralkyl aminoalkyl, N-alkyl-N-aryl aminoalkyl, aryloxy, aralkoxy, arylthio, aralkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-aryl aminosulfonyl, arylsulfonyl, N-alkyl-N-aryl aminosulfonyl;

or a pharmaceutically-acceptable salt thereof.

2. The method of Claim 1 wherein said 5-lipoxygenase inhibitor and said cyclooxygenase-2 inhibitor are administered in a sequential manner.

3. The method of Claim 1 wherein said 5-lipoxygenase inhibitor and said cyclooxygenase-2 inhibitor are administered in a substantially simultaneous manner.

4. The method of Claim 1 wherein the 5-lipoxygenase inhibitor is selected from masoprocol, tenidap, zileuton, flolufen, lonapalene, tagorizine, Abbott A-121798, Abbott A-76745, N'-[[5-(4-fluorophenoxy)furan-2-yl]-1-methyl-2-propynyl]-N'-hydroxyurea (Abbott A-78773), (R)(+)N'-[[5-(4-fluorophenoxy)furan-2-yl]-1-methyl-2-propynyl]-N-hydroxyurea (Abbott A-79175), Abbott ABT 761, Dainippon AL-3264, Bayer Bay-x-1005, Biofor BF-389, bunaprolast, Cytomed CMI-392, Takeda CV-6504, Efamol EF-40, Ciba-Geigy CGS-26529, enazadrem phosphate, Leo Denmark ETH-615, flezelastine hydrochloride, lonapalene, Merck Frosst L 663536, Merck Frosst L 699333, Merckle ML-3000, 3M Pharmaceuticals R-840, rilopirox, Schering Plough SCH 40120, tepoxalin, linazolast (TMK-688), Tanabe T-757, Tanabe T-799, Zeneca ZD 7717, Zeneca ZM-216800, Zeneca ZM 230487, and Zeneca ZD-2138.

5. The method of Claim 4 wherein the 5-lipoxygenase inhibitor is selected from tenidap, zileuton, flobufen, lonapalene, tagorizine, Abbott A-121798, Abbott A-76745, N'-[[5-(4-fluorophenoxy)furan-2-yl]-1-methyl-2-propynyl]-N'-hydroxyurea (Abbott A-78773), (R)(+)-N'-[[5-(4-fluorophenoxy)furan-2-yl]-1-methyl-2-propynyl]-N-hydroxyurea (Abbott A-79175), Abbott ABT 761, Ciba-Geigy CGS-26529, Biofor BF-389, Cytomed CMI-392, Leo Denmark ETH-615, lonapalene, Merck Frosst L 699333, Merckle ML-3000, 3M Pharmaceuticals R-840, linazolast (TMK-688), Tanabe T-757, Tanabe T-799, Zeneca ZD 7717, Zeneca ZM-216800, Zeneca ZM 230487, and Zeneca ZD-2138.

6. The method of Claim 1 wherein A is selected from oxazolyl, isoxazolyl, dihydrofuryl, imidazolyl, and pyrazolyl; wherein R¹ is selected from 5- and 6-membered heterocyclo, and aryl selected from phenyl, biphenyl and naphthyl, wherein R¹ is optionally substituted at a substitutable position with one or more radicals selected from lower alkyl, lower haloalkyl, cyano, carboxyl, lower alkoxy carbonyl, hydroxyl, lower hydroxyalkyl, lower haloalkoxy, amino, lower alkylamino, phenylamino, nitro, lower alkoxyalkyl, lower alkylsulfinyl, halo, lower alkoxy and lower alkylthio; wherein R² is amino; and wherein R³ is a radical selected from oxo, cyano, carboxyl, lower alkoxy carbonyl, lower carboxyalkyl, lower cyanoalkyl, halo, lower alkyl, lower alkyloxy, lower cycloalkyl, phenyl, lower haloalkyl, 5- or 6-membered heterocyclo, lower hydroxylalkyl, lower aralkyl, acyl, phenylcarbonyl, lower alkoxyalkyl, 5- or 6-membered heteroaryloxy, aminocarbonyl, lower alkylaminocarbonyl, lower alkylamino, lower aminoalkyl, lower alkylaminoalkyl, phenyloxy, and lower aralkoxy; or a pharmaceutically-acceptable salt thereof.

7. The method of Claim 6 wherein A is selected from oxazolyl, isoxazolyl, imidazolyl, and pyrazolyl; wherein R¹ is phenyl optionally substituted at a substitutable position with one or more radicals selected from methyl, ethyl, isopropyl, butyl, tert-butyl, isobutyl, pentyl, hexyl, trifluoromethyl, cyano, carboxyl, methoxycarbonyl, hydroxyl, hydroxymethyl, trifluoromethoxy, amino, N-methylamino, N,N-dimethylamino, N-ethylamino, N,N-dipropylamino, N-butylamino, N-methyl-N-ethylamino, nitro, methoxymethyl, methylsulfinyl, fluoro, chloro, bromo, methoxy, ethoxy, propoxy, n-butoxy, pentoxy, and methylthio; wherein R² is amino; and wherein R³ is a radical selected from oxo, cyano, carboxyl, methoxycarbonyl, ethoxycarbonyl, carboxypropyl, carboxymethyl, carboxyethyl, cyanomethyl, fluoro, chloro, bromo, methyl, ethyl, isopropyl, butyl, tert-butyl, isobutyl, pentyl, hexyl, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, fluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, methoxy, ethoxy, propoxy, n-butoxy, pentoxy, cyclohexyl, phenyl, pyridyl, thienyl, thiazolyl, oxazolyl, furyl, pyrazinyl, hydroxylmethyl, hydroxylpropyl, benzyl, formyl, phenylcarbonyl, methoxymethyl, furylmethyloxy, aminocarbonyl, N-methylaminocarbonyl, N,N-dimethylaminocarbonyl, N,N-dimethylamino, N-ethylamino, N,N-dipropylamino, N-butylamino, N-methyl-N-ethylamino, aminomethyl, N,N-dimethylaminomethyl, N-methyl-N-ethylaminomethyl, benzyloxy, and phenyloxy; or a pharmaceutically-acceptable salt thereof.

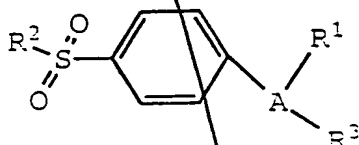
8. The method of Claim 7 selected from compounds, their prodrugs and their pharmaceutically-acceptable salts, of the group consisting of

3-(3,4-difluorophenyl)-4-(4-methylsulfonylphenyl)-
 2-(5H)-furanone;
 3-phenyl-4-(4-methylsulfonylphenyl)-2-(5H)-furanone;
 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-
 pyrazol-1-yl]benzenesulfonamide;
 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-
 pyrazol-1-yl]benzenesulfonamide;
 4-[5-(3-fluoro-4-methoxyphenyl)-3-
 (difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
 3-[1-[4-(methylsulfonyl)phenyl]-4-trifluoromethyl-
 1H-imidazol-2-yl]pyridine;
 2-methyl-5-[1-[4-(methylsulfonyl)phenyl]-4-
 trifluoromethyl-1H-imidazol-2-yl]pyridine;
 4-[2-(5-methylpyridin-3-yl)-4-(trifluoromethyl)-
 1H-imidazol-1-yl]benzenesulfonamide;
 4-[5-methyl-3-phenylisoxazol-4-
 yl]benzenesulfonamide;
 4-[5-hydroxyethyl-3-phenylisoxazol-4-
 yl]benzenesulfonamide;
 [2-trifluoromethyl-5-(3,4-difluorophenyl)-4-
 oxazolyl]benzenesulfonamide;
 4-[2-methyl-4-phenyl-5-
 oxazolyl]benzenesulfonamide; and
 4-[5-(3-fluoro-4-methoxyphenyl)-2-trifluoromethyl)-
 4-oxazolyl]benzenesulfonamide.

9. A combination comprising a therapeutically-effective amount of a cyclooxygenase-2 inhibitor, a 5-lipoxygenase inhibitor and an immunosuppressive drug selected from antiproliferative agents, antiinflammatory-acting compounds and inhibitors of leukocyte activation.

10. The combination of Claim 9 wherein the cyclooxygenase-2 inhibitor is selected from Dupont Dup-

697, Taisho NS-398, meloxicam, flosulide and compounds of Formula I



I

wherein A is a 5- or 6-member ring substituent selected from partially unsaturated or unsaturated heterocyclo and carbocyclic rings;

wherein R¹ is at least one substituent selected from heterocyclo, cycloalkyl, cycloalkenyl and aryl, wherein R¹ is optionally substituted at a substitutable position with one or more radicals selected from alkyl, haloalkyl, cyano, carboxyl, alkoxycarbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, arylamino, nitro, alkoxylalkyl, alkylsulfinyl, halo, alkoxy and alkylthio;

wherein R² is selected from alkyl, and amino; and

wherein R³ is a radical selected from halo, alkyl, alkenyl, alkynyl, oxo, cyano, carboxyl, cyanoalkyl, heterocyclooxy, alkylloxy, alkylthio, alkylcarbonyl, cycloalkyl, aryl, haloalkyl, heterocyclo, cycloalkenyl, aralkyl, heterocycloalkyl, acyl, alkylthioalkyl, hydroxyalkyl, alkoxycarbonyl, arylcarbonyl, aralkylcarbonyl, aralkenyl, alkoxylalkyl, arylthioalkyl, aryloxyalkyl, aralkylthioalkyl, aralkoxyalkyl, alkoxyaralkoxyalkyl, alkoxycarbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-arylaminocarbonyl, N-alkyl-N-arylaminocarbonyl, alkylaminocarbonylalkyl, carboxylalkyl, alkylamino, N-arylamino, N-aralkylamino, N-alkyl-N-aralkylamino, N-alkyl-N-arylamino, aminoalkyl, alkylaminoalkyl, N-arylaminalkyl, N-aralkylaminalkyl, N-alkyl-N-aralkylaminalkyl, N-alkyl-N-arylaminalkyl, aryloxy, aralkoxy, arylthio, aralkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-

arylaminosulfonyl, arylsulfonyl, N-alkyl-N-arylaminosulfonyl;

or a pharmaceutically-acceptable salt thereof.

- 5 11. The combination of Claim 9 wherein the 5-lipoxygenase inhibitor is selected from masoprocot, tenidap, zileuton, flobufen, lonapalene, tagorizine, Abbott A-121798, Abbott A-76745, N'-[[5-(4-fluorophenoxy)furan-2-yl]-1-methyl-2-propynyl]-N'-
- 10 hydroxyurea (Abbott A-78773), (R)(+)N'-[[5-(4-fluorophenoxy)furan-2-yl]-1-methyl-2-propynyl]-N-hydroxyurea (Abbott A-79175), Abbott ABT 761, Dainippon AL-3264, Bayer Bay-x-1005, Biofor BF-389, bunaprolast, Cytomed CMI-392, Takeda CV-6504, Efamol EF-40,
- 15 enazadrem phosphate, Leo Denmark ETH-615, flezelastine hydrochloride, Merck Frosst L 663536, Merckle ML-3000, 3M Pharmaceuticals R-840, rilopirox, Schering Plough SCH 40120, tepoxalin, linazolast (TMK-688), Tanabe T-757, Tanabe T-799, Zeneca ZD-2138, Abbott A 72694,
- 20 Abbott A-80263, Biofor BF-397, Bristol-Myers Squibb BU-4601A, carbazoycin C, lagunamycin, Wellcome BW-70C, Ciba-Geigy CGS-26529, Warner-Lambert CI 1004, Warner-Lambert PD-136005, Warner-Lambert PD-145246, Eisai E 3040, Fujirebio F-1322, Fisons FPL-64170, Fujisawa FR 110302, Nippon Hypox HX 0386, Merck & Co L-699333,
- 25 Merck Frosst L 739010, Lilly LY-269415, Lilly LY 178002, Meiji Milk MM-7002, Hoechst Roussel P 8892, Hoechst Roussel P 8977, SmithKline Beecham SB-202235, Green Cross SS-81-OH, Terumo Keio University TMK 685,
- 30 American Home Products WAY-121520, American Home Products WAY-125007, Zeneca ZD 7717, Zeneca ZM-216800, Zeneca ZM 230487, 1,2-dihydro-n-(2-thiazolyl)-1-oxopyrrolo(3,2,1-kl)phenothiazine-1-carboxamide, Abbott A-65260, Abbott A-69412, Abbott Abbott-63162, American
- 35 Home Products AHR-5333, Bayer Bay-q-1531, Boehringer Ingelheim BI-L-357, Boehringer Ingelheim BI-L-93BS, Boehringer Ingelheim BIL 226XX, Bristol-Myers Squibb

5 BMY-30094, carbazomycin B, Wellcome BW 4C, Wellcome BW-B218C, Wellcome BW-B70C, Chauvin CBS-1114, Ciba-Geigy CGS-21595, Ciba-Geigy CGS-22745, Ciba-Geigy CGS-23885, Ciba-Geigy CGS 24891, Ciba-Geigy CGS-8515, Chiesi CHF-1909, Warner-Lambert CI-986, Warner-Lambert CI 987, cirsilinol, docebenone, DuPont Merck DuP-654, Eisai E 5110, Eisai E-6080, Green Cross EN-105, enofelast, epocarbazolin-A, eprovafen, evandamine, forsythiaside, Fisons FPL 62064, Glaxo GR-80907, Zeneca ICI-211965, isoflavans, Kyowa Hakko KF-8940, Merck & Co L-651392, Merck & Co L-651896, Merck & Co L-652343, Merck & Co L-656224, Merck & Co L-670630, Merck & Co L-674636, Merck & Co L-691816, Lilly LY-233569, Lilly LY-280810, Merck & Co MK-591, Merck & Co MK-886, nitrosoxacin-A, Ono ONO-5349, Ono ONO-LP-219, Ono ONO-LP-269, Warner-Lambert PD-127443, Purdue Frederick PF-5901, Sandoz QA-208-199, Johnson & Johnson R-68151, Johnson & Johnson R-85355, Rhone-Poulenc Rorer Rev-5367, Rhone-Poulenc Rorer RG-5901-A, Rhone-Poulenc Rorer RG-6866, Roussel-Uclaf RU-46057, Searle SC-41661A, Searle SC-45662, Sandoz SDZ-210-610, SmithKline Beecham SK&F-104351, SmithKline Beecham SK&F-104498, SmithKline Beecham SK&F-105809, Synthelabo SL-81-0433, Teijin TEI-8005, Terumo TMK-777, Terumo TMK-781, Terumo TMK-789, Terumo TMK-919, Terumo TMK-992, Teikoku Hormone TZI-2721, Teikoku Hormone TZI-41127, American Home Products WAY-120739, American Home Products WY 47288, American Home Products Wy-48252, American Home Products Wy-50295, and Yoshitomi Y-19432.

12. The combination of Claim 11 wherein the 5-lipoxygenase inhibitor is selected from masoprocol, tenidap, zileuton, flubufen, lonapalene, tagorizine, Abbott A-121798, Abbott A-76745, N'-[[5-(4-fluorophenoxy)furan-2-yl]-1-methyl-2-propynyl]-N'-hydroxyurea (Abbott A-78773), (R)(+)N'-[[5-(4-fluorophenoxy)furan-2-yl]-1-methyl-2-propynyl]-N-

hydroxyurea (Abbott A-79175), Abbott ABT 761, Dainippon
AL-3264, Bayer Bay-x-1005, Biofor BF-389, bunaprolast,
Cytomed CMI-392, Takeda CV-6504, Efamol EF-40, Ciba-
Geigy CGS-26529, enazadrem phosphate, Leo Denmark ETH-
5 615, flezelastine hydrochloride, lonapalene, Merck
Frosst L 663536, Merck Frosst L 699333, Merckle ML-
3000, 3M Pharmaceuticals R-840, rilopirox, Schering
Plough SCH 40120, tepoxalin, linazolast (TMK-688),
Tanabe T-757, Tanabe T-799, Zeneca ZD 7717, Zeneca ZM-
10 216800, Zeneca ZM 230487, and Zeneca ZD-2138.

13. The combination of Claim 12 wherein the 5-
lipooxygenase inhibitor is selected from tenidap,
zileuton, flobufen, lonapalene, tagorizine, Abbott A-
15 121798, Abbott A-76745, N'-[[5-(4-fluorophenoxy)furan-
2-yl]-1-methyl-2-propynyl]-N'-hydroxyurea (Abbott A-
78773), (R)(+)N'-[[5-(4-fluorophenoxy)furan-2-yl]-1-
methyl-2-propynyl]-N'-hydroxyurea (Abbott A-79175),
Abbott ABT 761, Ciba-Geigy CGS-26529, Biofor BF-389,
20 Cytomed CMI-392, Leo Denmark ETH-615, lonapalene, Merck
Frosst L 699333, Merckle ML-3000, 3M Pharmaceuticals R-
840, linazolast (TMK-688), Tanabe T-757, Tanabe T-799,
Zeneca ZD 7717, Zeneca ZM-216800, Zeneca ZM 230487, and
Zeneca ZD-2138.

25 14. The combination of Claim 10 wherein A is
selected from oxazolyl, isoxazolyl, thienyl,
dihydrofuryl, furyl, pyrrolyl, pyrazolyl, thiazolyl,
imidazolyl, isothiazolyl, cyclopentenyl, phenyl, and
30 pyridyl; wherein R¹ is selected from 5- and 6-membered
heterocyclo, lower cycloalkyl, lower cycloalkenyl and
aryl selected from phenyl, biphenyl and naphthyl,
wherein R¹ is optionally substituted at a substitutable
position with one or more radicals selected from lower
35 alkyl, lower haloalkyl, cyano, carboxyl, lower
alkoxycarbonyl, hydroxyl, lower hydroxyalkyl, lower
haloalkoxy, amino, lower alkylamino, phenylamino,

nitro, lower alkoxyalkyl, lower alkylsulfinyl, halo,
lower alkoxy and lower alkylthio; wherein R^2 is selected
from lower alkyl and amino; and wherein R^3 is a radical
selected from halo, lower alkyl, oxo, cyano, carboxyl,
5 lower cyanoalkyl, heteroaryloxy, lower alkyloxy, lower
cycloalkyl, phenyl, lower haloalkyl, 5- or 6-membered
heterocyclo, lower hydroxylalkyl, lower aralkyl, acyl,
phenylcarbonyl, lower alkoxyalkyl, heteroaryloxy,
alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl,
10 alkylamino, aminoalkyl, alkylaminoalkyl, aryloxy, and
aralkoxy; or a pharmaceutically-acceptable salt
thereof.

15 15. The combination of Claim 14 wherein A is
selected from oxazolyl, isoxazolyl, dihydrofuryl,
imidazolyl, and pyrazolyl; wherein R^1 is selected from
5- and 6-membered heterocyclo, and aryl selected from
phenyl, biphenyl and naphthyl, wherein R^1 is optionally
substituted at a substitutable position with one or
20 more radicals selected from lower alkyl, lower
haloalkyl, cyano, carboxyl, lower alkoxycarbonyl,
hydroxyl, lower hydroxyalkyl, lower haloalkoxy, amino,
lower alkylamino, phenylamino, nitro, lower
alkoxyalkyl, lower alkylsulfinyl, halo, lower alkoxy
25 and lower alkylthio; wherein R^2 is amino; and wherein R^3
is a radical selected from oxo, cyano, carboxyl, lower
alkoxycarbonyl, lower carboxyalkyl, lower cyanoalkyl,
halo, lower alkyl, lower alkyloxy, lower cycloalkyl,
phenyl, lower haloalkyl, 5- or 6-membered heterocyclo,
30 lower hydroxylalkyl, lower aralkyl, acyl,
phenylcarbonyl, lower alkoxyalkyl, 5- or 6-membered
heteroaryloxy, aminocarbonyl, lower alkylaminocarbonyl,
lower alkylamino, lower aminoalkyl, lower
alkylaminoalkyl, phenyloxy, and lower aralkoxy; or a
35 pharmaceutically-acceptable salt thereof.

16. The combination of Claim 15 wherein A is selected from oxazolyl, isoxazolyl, imidazolyl, and pyrazolyl; wherein R¹ is phenyl optionally substituted at a substitutable position with one or more radicals selected from methyl, ethyl, isopropyl, butyl, tert-butyl, isobutyl, pentyl, hexyl, trifluoromethyl, cyano, carboxyl, methoxycarbonyl, hydroxyl, hydroxymethyl, trifluoromethoxy, amino, N-methylamino, N,N-dimethylamino, N-ethylamino, N,N-dipropylamino, N-butylamino, N-methyl-N-ethylamino, nitro, methoxymethyl, methylsulfinyl, fluoro, chloro, bromo, methoxy, ethoxy, propoxy, n-butoxy, pentoxy, and methylthio; wherein R² is amino; and wherein R³ is a radical selected from oxo, cyano, carboxyl, methoxycarbonyl, ethoxycarbonyl, carboxypropyl, carboxymethyl, carboxyethyl, cyanomethyl, fluoro, chloro, bromo, methyl, ethyl, isopropyl, butyl, tert-butyl, isobutyl, pentyl, hexyl, fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, fluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, methoxy, ethoxy, propoxy, n-butoxy, pentoxy, cyclohexyl, phenyl, pyridyl, thienyl, thiazolyl, oxazolyl, furyl, pyrazinyl, hydroxymethyl, hydroxylpropyl, benzyl, formyl, phenylcarbonyl, methoxymethyl, furylmethoxy, aminocarbonyl, N-methylaminocarbonyl, N,N-dimethylaminocarbonyl, N,N-dimethylamino, N-ethylamino, N,N-dipropylamino, N-butylamino, N-methyl-N-ethylamino, aminomethyl, N,N-dimethylaminomethyl, N-methyl-N-ethylaminomethyl, benzyloxy, and phenyloxy; or a pharmaceutically-acceptable salt thereof.

Subt
A 2
17. The combination of Claim 16 selected from compounds, their prodrugs and their pharmaceutically-acceptable salts, of the group consisting of

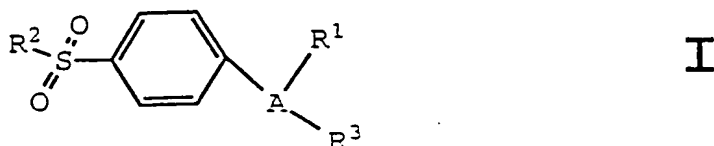
3-(3,4-difluorophenyl)-4-(4-methylsulfonylphenyl)-
 2-(5H)-furanone;
 3-phenyl-4-(4-methylsulfonylphenyl)-2-(5H)-furanone;
 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-
 5 pyrazol-1-yl]benzenesulfonamide;
 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-
 pyrazol-1-yl]benzenesulfonamide;
 4-[5-(3-fluoro-4-methoxyphenyl)-3-
 (difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide;
 10 3-[1-[4-(methylsulfonyl)phenyl]-4-trifluoromethyl-
 1H-imidazol-2-yl]pyridine;
 2-methyl-5-[1-[4-(methylsulfonyl)phenyl]-4-
 trifluoromethyl-1H-imidazol-2-yl]pyridine;
 4-[2-(5-methylpyridin-3-yl)-4-(trifluoromethyl)-
 15 1H-imidazol-1-yl]benzenesulfonamide;
 4-[5-methyl-3-phenylisoxazol-4-
 yl]benzenesulfonamide;
 4-[5-hydroxyethyl-3-phenylisoxazol-4-
 yl]benzenesulfonamide;
 20 [2-trifluoromethyl-5-(3,4-difluorophenyl)-4-
 oxazolyl]benzenesulfonamide;
 4-[2-methyl-4-phenyl-5-
 oxazolyl]benzenesulfonamide; and
 4-[5-(3-fluoro-4-methoxyphenyl)-2-trifluoromethyl)-
 25 4-oxazolyl]benzenesulfonamide.

18. The composition of Claim 9 wherein the leukocyte activation inhibitor is a cyclosporin.

30 19. The composition of Claim 18 wherein the
 C? cyclosporin is cyclosporin A.

20. A pharmaceutical composition comprising a
 pharmaceutically-acceptable carrier and a
 35 therapeutically-effective amount of a 5-lipoxygenase
 inhibitor, a cyclosporin and a cyclooxygenase-2

inhibitor selected from Dupont Dup 697, Taisho NS-398, meloxicam, flosulide and compounds of Formula I



5

wherein A is a 5- or 6-member ring substituent selected from partially unsaturated or unsaturated heterocyclo and carbocyclic rings;

wherein R¹ is at least one substituent selected from heterocyclo, cycloalkyl, cycloalkenyl and aryl, wherein R¹ is optionally substituted at a substitutable position with one or more radicals selected from alkyl, haloalkyl, cyano, carboxyl, alkoxy carbonyl, hydroxyl, hydroxyalkyl, haloalkoxy, amino, alkylamino, arylamino, nitro, alkoxyalkyl, alkylsulfinyl, halo, alkoxy and alkylthio;

wherein R² is selected from alkyl, and amino; and

wherein R³ is a radical selected from halo, alkyl, alkenyl, alkynyl, oxo, cyano, carboxyl, cyanoalkyl, heterocycloxy, alkyloxy, alkylthio, alkylcarbonyl, cycloalkyl, aryl, haloalkyl, heterocyclo, cycloalkenyl, aralkyl, heterocycloalkyl, acyl, alkylthioalkyl, hydroxyalkyl, alkoxy carbonyl, arylcarbonyl, aralkylcarbonyl, aralkenyl, alkoxyalkyl, arylthioalkyl, aryloxyalkyl, aralkylthioalkyl, aralkoxyalkyl, alkoxyaralkoxyalkyl, alkoxy carbonylalkyl, aminocarbonyl, aminocarbonylalkyl, alkylaminocarbonyl, N-arylaminocarbonyl, N-alkyl-N-arylaminocarbonyl, alkylaminocarbonylalkyl, carboxyalkyl, alkylamino, N-aryl amino, N-aralkylamino, N-alkyl-N-aralkylamino, N-alkyl-N-aryl amino, aminoalkyl, alkylaminoalkyl, N-aryl aminoalkyl, N-aralkylaminoalkyl, N-alkyl-N-aralkylaminoalkyl, N-alkyl-N-aryl aminoalkyl, aryloxy, aralkoxy, arylthio, aralkylthio, alkylsulfinyl, alkylsulfonyl, aminosulfonyl, alkylaminosulfonyl, N-

arylaminosulfonyl, arylsulfonyl, N-alkyl-N-arylaminosulfonyl;

or a pharmaceutically-acceptable salt thereof.

5 21. The method of Claim 2 further characterized
by suppressing immune response in a subject susceptible
to or afflicted with rejection of an organ transplanted
to said subject; graft versus host disease; an
autoimmune disease, an inflammatory disease, or a
10 condition with underlying autoimmune or inflammatory
reactivities or responses; an allergy; asthma; airway
hypersensitivity; septic shock; myasthenia gravis;
autoimmune thyroiditis; Grave's disease; autoimmune
hemolytic anemia; autoimmune thrombocytopenia purpura;
15 mixed connective tissue disease; idiopathic Addison's
disease; Sjogren's syndrome; urticaria; an acute
hypersensitivity response or a delayed hypersensitivity
response; Goodpasture's syndrome; hemolytic anemia;
contact dermatitis; granuloma; antibody-induced
20 thrombocytopenia; hypersensitivity pneumonitis;
glomerulonephritis; thyroiditis; encephalomyelitis; or
meningitis.